UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/926,299	10/09/2001	Yoshiya Gunji	212289US0PCT	4922

38108 7590 09/21/2006

CERMAK & KENEALY LLP
ACS LLC
515 EAST BRADDOCK ROAD
SUITE B
ALEXANDRIA, VA 22314

EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/926,299	GUNJI ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2006 and 10 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5,7-10 and 12-34* is/are pending in the application.

4a) Of the above claim(s) *14,15,18,19 and 22-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,7-10,12,13 and 26-34* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☒ Claim(s) *16,20 and 21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 1-2, 5, 7-10, 12-34 are pending in the application.

[2] Applicant's amendments to the claims, filed on 6/30/2006 and 7/10/2006, are acknowledged. The claim listing filed on 6/30/2006 fails to satisfy the requirements of 37 CFR 1.121 for the reason(s) set forth in the Office communication mailed on 7/5/2006. The claim listing filed on 7/10/2006 replaces all prior versions and listings of the claims.

[3] Applicant's arguments filed on 6/30/2006 have been fully considered and are deemed to be persuasive to overcome some of the objections and/or rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

[5] In order to clarify the record, it is noted that the examiner inadvertently indicated that claims 1-2, 5, 7-10, 12-13, 16-17, and 20-31 were pending in the prior Office action, thereby omitting pending claims 14-15 and 18-19. Because the claim text was not presented for claims 14-15 and 18-19 in the claim listing filed on 12/15/2005, the examiner mistakenly held these claims as canceled. According to the current claim listing, it is clear that claims 1-2, 5, 7-10, 12-34 are pending. This inadvertent oversight did not affect the examination of the claims as the omitted pending claims were properly withdrawn from consideration.

Lack of Unity

[6] Claims 14-15, 18-19, and 22-25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/14/2004.

[7] Claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-34 are being examined on the merits.

Claim Objection(s)

[8] Claim 17 is objected to in the recitation of "enoded," which would appear to be a misspelling of "encoded." Appropriate correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

[9] The written description rejection of claims 1-2, 5, 7-10, 12-13, and 26-31 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action. Newly added claims 32-34 are included in the instant rejection. Thus, claims 1-2, 5, 7-10, 12-13, 16-17, 20-21, and 26-34 are rejected herein.

RESPONSE TO ARGUMENT: Beginning at p. 11, middle of the instant response, applicant argues the specification discloses three well-known methods for enhancing the recited protein activities, which are asserted to be sufficient to describe all possible methods of enhancing protein activity as encompassed by the claims.

Applicant argues that the three disclosed methods are sufficiently divergent to demonstrate possession of the claimed invention. According to applicant, the examiner is improperly requiring applicant to describe all possible methods of enhancing protein activity.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification fails to adequately describe the claimed genus of *M. methylotrophus* strains, particularly with respect to the characteristic of having enhanced dihydrodipicolinate synthase activity and/or aspartokinase activity and optionally enhanced activities of a genus of aspartic acid semialdehyde dehydrogenases, dihydrodipicolinate reductases, and/or diaminopimelate decarboxylases. According to MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. While the examiner acknowledges applicant's disclosed methods for enhancing expression and activity of a polypeptide in

a strain of *M. methylotrophus,* the claims encompass widely variant strains of *M. methylotrophus* that has enhanced activity of dihydrodipicolinate synthase and/or aspartokinase activity and optionally enhanced activity of semialdehyde dehydrogenases, dihydrodipicolinate reductases, and/or diaminopimelate decarboxylases, homoserine dehydrogenases, homoserine kinases, and threonine synthases, wherein the activity is enhanced by *any* method or mechanism, including, *e.g.,* mutation of the dihydrodipicolinate synthase and/or aspartokinase and optionally mutation of the semialdehyde dehydrogenase, dihydrodipicolinate reductase, diaminopimelate decarboxylase, homoserine dehydrogenase, homoserine kinase, and/or threonine synthase encoding nucleic acid that results in, *e.g.,* 1) decreased degradation due to stabilization of mRNA and/or protein, 2) increased rate of enzymatic activity, 3) reduced feedback inhibition, 4) increased endogenous promoter activity or altering transcriptional regulatory proteins to up-regulate the endogenous expression of the above-listed enzymes or a combination of these methods. In this case, the specification fails to describe any specific alterations to SEQ ID NO:10 and/or 6 or semialdehyde dehydrogenase, dihydrodipicolinate reductase, diaminopimelate decarboxylase, homoserine dehydrogenase, homoserine kinase, and/or threonine synthase that result in an enhanced stability of mRNA/protein, increased rate of enzymatic activity, reduced feedback inhibition, any specific alterations to the endogenous transcriptional elements controlling expression of SEQ ID NO:10 and/or 6 or semialdehyde dehydrogenase, dihydrodipicolinate reductase, diaminopimelate decarboxylase, homoserine dehydrogenase, homoserine kinase, and/or threonine

synthase or any specific alterations to transcriptional regulatory proteins that regulate the endogenous expression of the above-listed enzymes to achieve enhanced activity of the recited enzyme activities. In this case, the disclosed *M. methylotrophus* strain with enhanced enzyme activity fails to reflect the variation among the members of the genus.

Given the lack of description of a representative number of *M. methylotrophus* strains as encompassed by the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[10] The scope of enablement rejection of claims 1-2, 5, 7-8, 10, 12-13, and 26-31 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record and the reasons stated below. The rejection was fully explained in a prior Office action. Newly added claims 32-34 are included in the instant rejection. Thus, claims 1-2, 5, 7-8, 10, 12-13, 16-17, 20-21, and 26-34 are rejected herein.

RESPONSE TO ARGUMENT: Beginning at p. 12, middle of the instant response, applicant argues the specification discloses three well-known methods for enhancing the recited protein activities, which are asserted to be sufficient to enable all possible methods of enhancing protein activity as encompassed by the claims. Applicant argues that the three disclosed methods are sufficiently divergent to demonstrate enablement of the full scope of the claimed invention. According to applicant, the examiner is improperly requiring applicant to describe all possible methods of enhancing protein activity.

Applicant's argument is not found persuasive. The examiner maintains the position that the specification fails to enable all *M. methylotrophus* strains as broadly encompassed by the claims, particularly with respect to the characteristic of having enhanced dihydrodipicolinate synthase activity and/or aspartokinase activity and optionally enhanced activities of a genus of aspartic acid semialdehyde dehydrogenases, dihydrodipicolinate reductases, and/or diaminopimelate decarboxylases. While the examiner acknowledges applicant's disclosed methods for enhancing expression and activity of a polypeptide in a strain of *M. methylotrophus,* the breadth of the claims encompasses strains of *M. methylotrophus* that have enhanced activity of dihydrodipicolinate synthase and/or aspartokinase activity and optionally enhanced activity of semialdehyde dehydrogenases, dihydrodipicolinate reductases, and/or diaminopimelate decarboxylases, homoserine dehydrogenases, homoserine kinases, and threonine synthases, wherein the activity is enhanced by *any* method or mechanism, including, *e.g.,* mutation of the dihydrodipicolinate synthase and/or aspartokinase and optionally mutation of the semialdehyde dehydrogenase, dihydrodipicolinate reductase, diaminopimelate decarboxylase, homoserine dehydrogenase, homoserine kinase, and/or threonine synthase encoding nucleic acid that results in, *e.g.,* 1) decreased degradation due to stabilization of mRNA and/or protein, 2) increased rate of enzymatic activity, 3) reduced feedback inhibition, 4) increased endogenous promoter activity or altering transcriptional regulatory proteins to up-regulate the endogenous expression of the above-listed enzymes or a combination of these methods. In this case, the specification fails to describe any specific alterations

to SEQ ID NO:10 and/or 6 or semialdehyde dehydrogenase, dihydrodipicolinate reductase, diaminopimelate decarboxylase, homoserine dehydrogenase, homoserine kinase, and/or threonine synthase that result in an enhanced stability of mRNA/protein, increased rate of enzymatic activity, reduced feedback inhibition, any specific alterations to the endogenous transcriptional elements controlling expression of SEQ iD NO:10 and/or 6 or semialdehyde dehydrogenase, dihydrodipicolinate reductase, diaminopimelate decarboxylase, homoserine dehydrogenase, homoserine kinase, and/or threonine synthase or any specific alterations to transcriptional regulatory proteins that regulate the endogenous expression of the above-listed enzymes to achieve enhanced activity of the recited enzymes. In this case, the disclosed working example of an *M. methylotrophus* strain with enhanced enzyme activity along with the state of the art at the time of the invention fail to provide the necessary guidance for making all *M. methylotrophus* strains with enhanced enzyme activity as encompassed by the claims. Without such guidance, it is highly unpredictable as to which mutations within the enzyme's gene sequence can be made with an expectation of achieving enhanced activity, which is undisputed by applicant. While methods for increasing enzyme activity in a host cell were well-known, certain of these methods as encompassed by the claims require guidance *specific* to a particular enzyme and without such guidance, making all strains of *M. methylotrophus* as encompassed by the claims would require undue experimentation.

Claim Rejections - 35 USC § 102

[11] The rejection of claims 16 and 20 under 35 U.S.C. 102(b) as being anticipated by Kojima et al. (WO 95/16042; cited in the IDS filed 9/5/2003) is withdrawn in view of the claim amendment to limit the protein to comprising "the amino acid sequence" of SEQ ID NO:6 or 10 or variants thereof as encompassed by the claims.

Conclusion

[12] Status of the claims:

Claims 1-2, 5, 7-10, and 12-34 are pending.

Claims 14-15, 18-19, and 22-25 are withdrawn from consideration.

Claims 1-2, 5, 7-10, 12-13, and 26-34 are rejected.

Claim 17 would be allowable if rewritten or amended to overcome the objection(s) set forth in this Office action.

Claims 16 and 20-21 appear to be in condition for allowance.

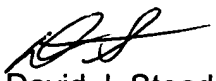
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656